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PRINCIPAL INVESTIGATOR: Andrew Berchuck, M.D.

CONTRACTING ORGANIZATION: Duke University Medical Center
Durham, North Carolina 27710

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Andrew Berchuck, M.D.

7. PERFORMING ORGANIZATION NAME(S) AND ADDRESS(ES)
Duke University Medical Center
Durham, North Carolina 27710

E-MAIL: berch001@mc.duke.edu

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13. ABSTRACT ***(Maximum 200 Words)***
Since reduction of ovulation is protective against ovarian cancer, prevention may represent a feasible approach to decreasing mortality. To achieve a better understanding of the etiology of ovarian cancer, which will translate into more effective chemoprevention strategies, we have initiated a molecular epidemiologic study in North Carolina. The study will consider genetic susceptibility, reproductive/hormonal and other exposures and acquired genetic alterations. The award from the DOD has been supplemented by a grant from the NCI allowing us to increase the number of cases and controls included; and the study will now be population-based with subjects recruited from 48 counties of central North Carolina. Subjects are interviewed in their homes, rather than by telephone, and about 200 women with ovarian cancer and 200 controls have been accrued thus far. Blood and cancer samples have been collected and DNA extracted and molecular analyses of p53, c-*myc* and genetic polymorphisms have recently commenced. Because progestins have a potent apoptotic effect on ovarian epithelial cells, the use of levonorgestrel in chemoprevention of ovarian cancer is being explored in chickens and women. A chemoprevention trial is ongoing in chickens and we will begin a trial to determine whether levonorgestrel induces apoptosis in the ovarian epithelium of women undergoing oophorectomy.

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Introduction

Ovarian cancer is the fourth leading cause of cancer deaths among women in the United States. There are three potential approaches to decreasing ovarian cancer mortality: screening and early detection, more effective treatment and prevention. All of these avenues should be explored, but we believe that prevention represents the most feasible approach. The rationale for prevention is derived from epidemiologic studies that have examined the relationship between reproductive history, hormone use and ovarian cancer. It has been convincingly demonstrated that reproductive events which reduce lifetime ovulatory cycles are protective. Although most women are unaware of this protective effect, those who use oral contraceptive pills for more than 5 years or have 3 children decrease their risk of ovarian cancer by greater than 50%. The biological mechanisms that underlie the association between ovulation and ovarian cancer are poorly understood, however. Our multidisciplinary ovarian cancer research group has been actively involved in studies that seek to elucidate the etiology of ovarian cancer and to translate this knowledge into effective preventive strategies. Joint consideration of genetic susceptibility, reproductive/hormonal and other exposures, acquired alterations in oncogenes and tumor suppressor genes and protective mechanisms such as apoptosis is required to accomplish this goal. We have initiated a molecular epidemiologic study of ovarian cancer in North Carolina to address the complex etiology of ovarian cancer. In addition, we are actively involved in development of chemopreventive strategies. We have performed a study in primates that suggests that the oral contraceptive has a potent apoptotic effect on the ovarian epithelium, mediated by the progestin component. In addition, in subsequent studies performed *in vitro*, we have induced apoptosis in epithelial cells treated with the progestin levonorgestrel. Progestin mediated apoptotic effects may be a major mechanism underlying the protection against ovarian cancer afforded by OCP use. This forms the basis for an investigation of the progestin class of drugs as chemopreventive agents for epithelial ovarian cancer. Currently studies to test the progestin levonorgestrel are underway in chickens and women.

Body

Projects 1 and 2: Molecular-epidemiology of ovarian cancer

With the support of the Department of Defense Ovarian Cancer Research Program we have initiated a molecular epidemiologic study of ovarian cancer to work towards the goal of a better understanding of the etiology of ovarian cancer. Drs. Andrew Berchuck (Gynecologic Oncologist) and Joellen Schildkraut (Epidemiologist) are working together to lead this study. Our initial plan was to accrue frozen tumor tissue and blood from 500 epithelial ovarian cancer cases treated at Duke University, the University of North Carolina at Chapel Hill and East Carolina University. In addition, 500 age and race-matched control subjects were to be accrued and both cases and controls were to be interviewed by telephone regarding known risk factors for ovarian cancer. After funding to support this project was received from the Department of Defense with Dr Berchuck as PI, additional funding was received to support this project from the NCI with Dr Schildkraut as PI. The additional funding has allowed us to increase the scope of the study. We will now be having nurse interviewers visiting the homes of all the cases and controls to administer the study questionnaire. Research subjects will be accrued from a

48 county region of central North Carolina using a rapid cases ascertainment mechanism established through the state tumor registry (see outlined area on map in appendix). Prior to initiating the study, we had to go through the process of IRB approval in each of the various hospitals involved (see newsletter in appendix). Treating physicians are contacted by mail to request permission to approach potential research subjects. A letter is sent inviting a woman to participate only if permission to contact is granted. Three nurse interviewers have been hired and trained and the research questionnaire was field tested on 20 women with ovarian cancer. Final revisions to the questionnaire were made before the study began to accrue actual research subjects. To date about 200 women with newly diagnosed ovarian cancer and 200 controls have been interviewed for the study. The investigators have had project meetings every other week with all the research staff to review progress and address ongoing issues and at this point we are very pleased with the accrual rate and other procedural aspects of the study. All clinical, epidemiologic and molecular data are stored as they are obtained in a computerized database.

During the interview a thorough history of the menstrual cycle and reproductive experiences of the study participants is obtained assisted by the use a life-time calendar method. In addition, information on oral contraceptives and hormone replacement therapy is obtained. Data on the family history of cancer, other risk factors, and potential confounders is also collected. The interview takes 60-90 minutes to complete. The interactions between the nurses and subjects has been uniformly positive (see newsletter in appendix). The women with ovarian cancer are highly motivated to talk about their history and have a high level of interest in supporting a study aimed at increasing our understanding of the causes of ovarian cancer. They greatly appreciate the opportunity to talk with a nurse who is truly interested in hearing all the details of their life experience. Blood and cancer samples have been collected, and DNA extracted and molecular analyses of the p53 tumor suppressor gene, c-*myc* and genetic polymorphisms have recently commenced. In cases in which fresh frozen ovarian cancer tissue is not available, consent has been obtained to procure paraffin blocks. Hopefully, in the next year we will have the opportunity to begin correlating molecular and epidemiologic data from the first few hundred cases and controls. This will allow us to address the goals of the specific aims outlined in this project.

Previously, using ovarian cancer cases and controls from the CASH study, we found a strong association between high lifetime ovulatory exposure and alteration of the p53 tumor suppressor gene. In project 1 of this proposal, directed by Dr. Berchuck (Gynecologic Oncologist), we are seeking to confirm the association between high lifetime ovulatory exposure and alterations in p53. More broadly, we will attempt to demonstrate that alterations in specific genes (eg, p53, HER-2/*neu*) serve as molecular signatures of distinct etiologic pathways and allow definition of more homogenous subsets of ovarian cancer. This could be critical as we strive to develop prevention strategies, as the optimal means of prevention may vary between different subsets of these cancers. In project 2, initially under the direction of Dr. Futreal (Molecular Geneticist), we are examining the role of genetic susceptibility in the development of ovarian cancer. More recently, Dr. Futreal has left Duke and this project is now being led by Jeffrey Marks, Ph.D. (Molecular Biologist). Drs. Berchuck and Marks are co-

directors of the Duke Comprehensive Cancer Center Breast/Ovarian Cancer Program and have a long track record of scientific collaboration over the past 10 years (see Dr Marks' CV in appendix). Although most of the genes responsible for dominant hereditary ovarian cancer syndromes (eg. BRCA1) likely have been discovered, there is evidence to suggest that polymorphisms in other genes may also affect cancer susceptibility in a more weakly penetrant fashion. Dr. Marks will investigate whether genetic polymorphisms affect ovarian cancer susceptibility. These studies will focus on genes involved in hormone and carcinogen metabolism. Since the effect of cancer susceptibility genes may be modified by other genes and exposures, he also will determine whether gene-gene and gene-environment interactions affect ovarian cancer susceptibility. Because of the low incidence of ovarian cancer, the ability to identify "high risk" subsets of women is critical if we hope to translate our emerging understanding of the etiology of ovarian cancer into effective prevention strategies.

Project 3: chemoprevention

Project 3 is under the direction of Gustavo Rodriguez, M.D. (Gynecologic Oncologist). The prevention strategy outlined in our proposal is based on the observation that progestins have a potent apoptotic effect on ovarian epithelial cells. With regard to cancer prevention, the apoptosis pathway is one of the most important *in vivo* mechanisms that functions to eliminate cells that have sustained DNA damage and which are thus prone to malignant transformation. In addition, a number of well known chemopreventive agents have been demonstrated to activate the apoptosis pathway in the target tissues that they protect from neoplastic transformation. We have performed a study in primates that suggests that the oral contraceptive has a potent apoptotic effect on the ovarian epithelium, mediated by the progestin component. In addition, in subsequent studies performed *in vitro*, we have induced apoptosis in transformed, immortalized, cultured human ovarian epithelial cells treated with the progestin levonorgestrel. This suggests that progestins may have a direct apoptotic effect on the ovarian epithelium. The finding that progestins activate this critical pathway in the ovarian epithelium, the site where ovarian cancers arise, makes it likely that progestin mediated apoptotic effects are a major mechanism underlying the protection against ovarian cancer afforded by routine OCP use. This forms the basis for an investigation of the progestin class of drugs as chemopreventive agents for epithelial ovarian cancer.

The studies outlined in our prevention grant are designed to add further support to notion that progestins are potent apoptotic agents on human ovarian epithelial cells, and to directly test the hypothesis in an animal model that progestins confer preventive effects against ovarian cancer. These aims in the grant are: (1) to evaluate the apoptotic effect of progestins on the human ovarian epithelium *in vivo*, (2) elucidate the molecular mechanisms by which progestins induce apoptosis in ovarian epithelial cells, and (3) to directly test the hypothesis that progestins confer preventive effects against ovarian cancer in a chemoprevention trial in the chicken, the only animal species with a high incidence of ovarian cancer.

In search of biologic effects of OCP's that have the potential to confer protective effects against ovarian cancer, we performed a 3-year study in primates that suggests that

oral contraceptive progestin markedly induces programmed cell death (apoptosis) in the ovarian epithelium and that this is highly associated with up-regulation of Transforming Growth Factor-Beta (TGF-β). These two molecular events have been strongly implicated in cancer prevention *in vivo*, and are believed to underlie the protective effects of other well-known chemopreventive agents such as the retinoids and Tamoxifen. In subsequent studies performed *in vitro*, we have induced apoptosis in immortalized, cultured human ovarian epithelial cells treated with progestin suggesting that progestins may have a direct apoptotic effect on the ovarian epithelium. We have recently completed a two-year prevention trial in the chicken (the only known animal with a high incidence of spontaneous ovarian adenocarcinoma) designed to test the hypothesis that progestins confer prevention against ovarian cancer. Two thousand two year-old birds were randomized into several groups, including untreated controls, and groups receiving progestin (Provera or levonorgestrel). Preliminary results suggest that at the two-year mark, chickens in groups treated with progestin contained 35% fewer ovarian and oviductal tumors than controls.

Given our preliminary data, we hypothesize that OCP progestins induce apoptosis in the human ovarian epithelium, and that induction of apoptosis is possibly mediated by TGF-β. With regard to cancer prevention, the apoptosis pathway is one of the most important *in vivo* mechanisms that functions to eliminate cells that have sustained DNA damage and which are thus prone to malignant transformation. In addition, a number of well-known chemopreventive agents have been demonstrated to activate the apoptosis pathway in the target tissues that they protect from neoplastic transformation. The finding that progestins activate this critical pathway in the ovarian epithelium raises the possibility that progestin-mediated apoptotic effects underlie the protection against ovarian cancer afforded by routine OCP use rather than inhibition of ovulation as has been previously suggested. This forms the basis, in our opinion, for further investigation of progestins as chemopreventive agents for ovarian cancer.

Key research accomplishments

This project is in its early developmental stage. The results of these studies will mature and be reported in the future.

Reportable outcomes

None to date.

Conclusions

The studies initiated by our program will enable us to define more homogeneous subsets of ovarian cancer based on epidemiologic and molecular characteristics, to identify women who are at increased risk for this disease and to develop chemopreventive strategies designed to decrease ovarian cancer incidence and mortality.

References

None

Appendices

April 2000 —Vol. 1, No. 2

North Carolina Ovarian Cancer Study

PURPOSE OF STUDY

To identify the environmental, reproductive, and genetic factors that contribute to the development of ovarian cancer.

STUDY PERIOD

January 1999-2003

OVARIAN CANCER STATISTICS

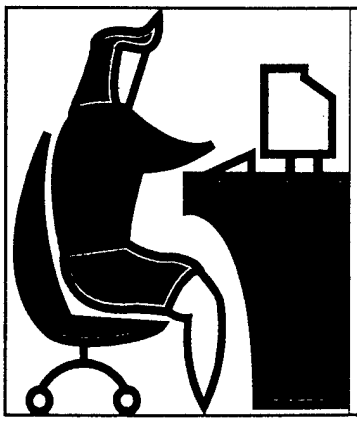
- ♀ **In cases where ovarian cancer is detected before it has spread beyond the ovaries, over 91% of women will survive longer than 5 years.**
- ♀ **Only 24% of ovarian cancer cases in the U.S. are diagnosed in the beginning stages.**
- ♀ **There is no reliable, simple-to-administer screening tool to detect ovarian cancer.**

Why Rapid-Case Ascertainment?

The North Carolina Ovarian Cancer Study is a population-based study being conducted in a 48-county region in this state. Our goal is to enroll 700 women with ovarian cancer and 700 women without ovarian cancer over a 4-year period.

In epidemiologic case-control studies such as this one, the objective is to understand disease causation by identifying the environmental, reproductive and genetic factors that contribute to the development of the disease. As time passes, the chance of including any one patient in the study decreases due to the high mortality rate associated with this disease. Therefore, it is critical that we identify newly diagnosed patients with ovarian cancer in a timely manner, with the goal of conducting an in-person interview within six months of the diagnosis. If only ovarian cancer survivors were enrolled, this would become a study of factors related to a mild form of ovarian cancer, or perhaps a better prognosis, rather than one of risk factors for developing this disease. We would be unable to distinguish effects of risk factors on the incidence of ovarian cancer from effects of risk factors on disease duration.

A system for rapid-case ascertainment has been implemented to facilitate identification of women with newly diagnosed epithelial ovarian cancer within a few months of their diagnosis. Hospital cancer registrars are asked to report all newly diagnosed epithelial ovarian cancer cases between the ages of 20 and 74 to the North Carolina Central Cancer Registry within one to two months of diagnosis, rather than according to the normal quarterly reporting periods. ♀



Resources on the Web

- ✦ National Ovarian Cancer Coalition
  www.ovarian.org
- ✦ Women's Cancer Network
  www.wcn.org
- ✦ OncoLink: Ovarian Cancer
  www.oncolink.upenn.edu

Witnessing

Robin Berger, RN
Nancy Fisher, RN

In a recent lecture at Duke University, Dr. Arthur Frank, author of *The Wounded Storyteller: Body, Illness, and Ethics* and a cancer survivor himself, discussed the need of the 'deeply ill' to have a witness to their story. Dr. Frank believes that the seriously ill, i.e., those who live with the idea that they may soon die from their disease, fear that their story will go unwitnessed and that their suffering will be in vain. But the act of storytelling provides the cancer patient with a connection to the future. Someone has listened to their story and will share their story, keeping their memory alive.

Three nurse-interviewers for the North Carolina Ovarian Cancer Study travel from Charlotte to New Bern, from Henderson to Lumberton and to the rural towns in between to hear the stories of women with ovarian cancer. Women are interviewed in their homes about their medical and reproductive history and their family's history of cancer, among other things. A detailed history of symptoms and doctor visits occurring in the year prior to their diagnosis allows each woman a chance to 'tell her story'.

"... the act of storytelling provides the cancer patient with a connection to the future."

Most women are eager to be interviewed and feel they are contributing to the wellbeing of future generations. One participant, who initially voiced uncertainty about participating, later admitted that her fear came from not knowing what to expect or how she would feel in discussing her medical history. Following the interview, she confessed that telling her story had been therapeutic. She reported that she donated the money she received for participating in memory of a young healthcare provider who had also had cancer. "The timing for everything just seemed right, and it was my way of giving back as a result of someone giving to me."

Another participant was particularly grateful for the opportunity to be in the study. She had no children or family and went through surgery and chemotherapy alone, having lost her husband to prostate cancer only two weeks before her diagnosis: she listed her minister as her closest relative. "Folks don't realize how appreciated a home-visit can be when you deal with cancer all on your own." She still has the "very nice" letter she received from the nurse after her interview and has said that she would be happy to do anything she could to further efforts in cancer research in the future.

We are gratified and awed by the stories these women share. We are appreciative of the time and support that participants, both cases and controls, have so freely given. Most of all, we are inspired by the spirit of service to others so pervasive among the many women who have taken part in the North Carolina Ovarian Cancer Study. ♀

Ovarian Cancer

By
Marilyn F. Vine, Ph.D.

Listen to me; I'm cancer free.
Or so I thought the truth to be.
To my surprise, a lump grapefruit size
had grown on my ovary.

Signs were there, but not so rare.
Little did I know that I should care.
Bloating and gas, common symptoms that pass,
lasted longer than I could bear.

My doctor was wise. Before I did rise,
he performed a pelvic exam.
Then on ultrasound, a tumor was found.
It wasn't my gallbladder. Damn!

Surgery, chemotherapy,
treatments of choice the experts agree.
Not too much fun, but the battle is won,
at least temporarily.

No screening test is considered the best.
So, be aware of signs that may manifest.
If symptoms last, see a doctor real fast
and pray for a better lab test.

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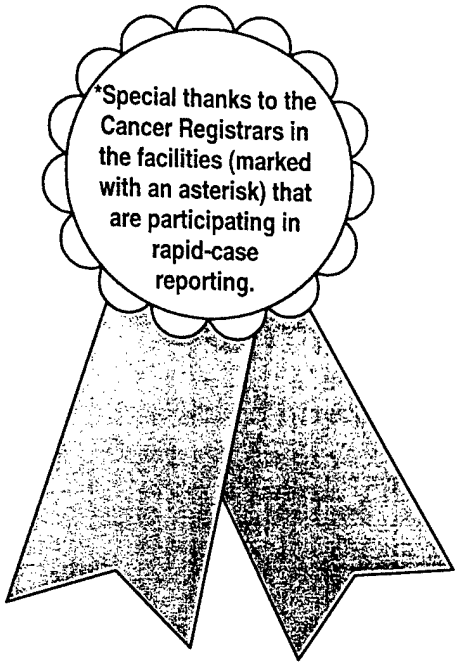
Thanks For Your Support!

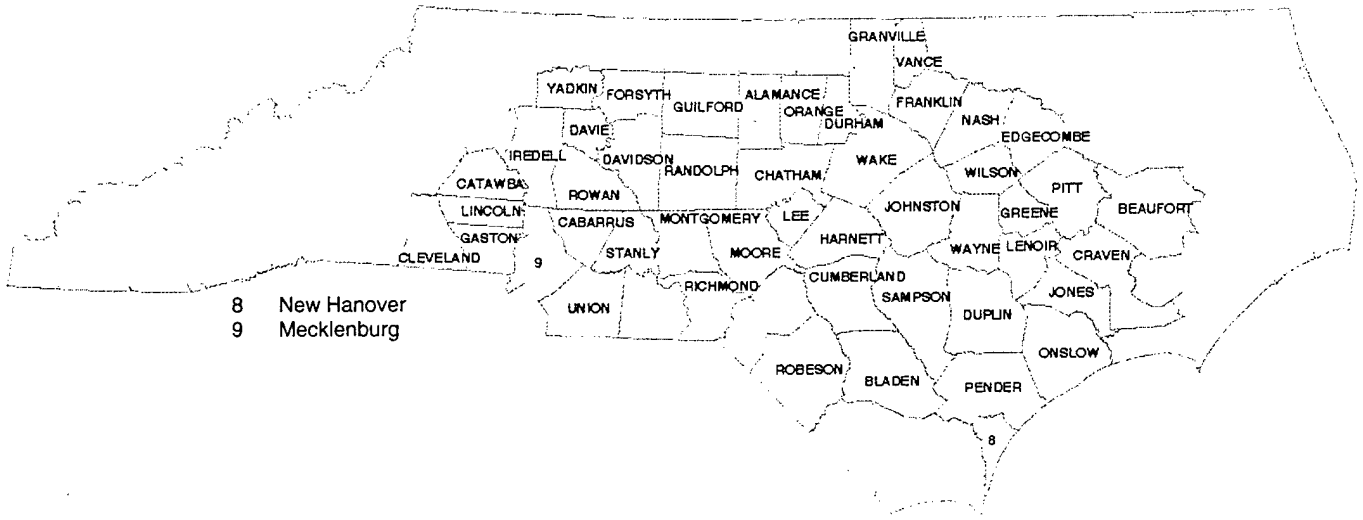
We would like to thank the following facilities for their approval of our study:



Alamance Regional Medical Center*
Betsy Johnson Memorial Hospital*
Bladen County Hospital*
Cape Fear Memorial Hospital*
Cape Fear Valley Health System*
Carolinas Medical Center*
Catawba Memorial Hospital*
Central Carolinas Medical Center*
Chatham Hospital*
Cleveland Regional Medical Center*
Community General Hospital*
Craven Medical Center*
Duke Medical Center*
Duplin General Hospital*
Durham Regional Hospital
First Health Moore Regional Center*
Forsyth Medical Center-Novant Health*
Granville Medical Center*
Heritage Hospital*
High Point Regional Hospital*
Iredell Memorial Hospital*
Kings Mountain Hospital*
Lake Norman Regional Medical Center
Lexington Memorial Hospital
Lincoln Regional Medical Center*
Maria Parham Hospital*
Medical Park Hospital-Novant Health*
Mercy Hospital*
Mercy Hospital South*
Moses H. Cone Memorial Hospital*
Nash Health Care*
Naval Hospital Cherry Point*
New Hanover Regional Medical Center*
Northeast Medical Center*
Pender Memorial Hospital*
Pitt County Memorial Hospital (ECU)*
Presbyterian Hospital-Novant Health*
Presbyterian Matthews-Novant Health*
Presbyterian Oncology & Assoc.
Pungo District Hospital*
Raleigh Community Hospital*
Richmond Memorial Hospital*
Rowan Regional Medical Center*
Sampson Regional Medical Center*
Stanly Memorial Hospital*
Union Memorial Hospital
University Hospital*
UNC Hospitals*
SCARC Seymour Johnson AFB
WakeMed
Western Wake Medical Center

48-County Study Area

If you are in the Study Area and would like your hospital to participate
Call Mary Beth Bell, 1-888-246-1250



Getting the Word Out

Since our last newsletter, North Carolina Ovarian Cancer Study staff have been very busy raising public awareness around the state about ovarian cancer and about our research. Newspaper articles regarding the study have appeared in Durham's *Herald-Sun* (September 19, 1999) and in Greensboro's *News & Record* (December 28, 1999). In the Fall, Dr. Joellen Schildkraut, Principal Investigator, was interviewed on the PBS television program, *"North Carolina Now."* She discussed risk factors associated with ovarian cancer and the importance of our research. OB-GYN Oncologist, Dr. Andrew Berchuck, Co-Investigator, has given a number of seminars on ovarian cancer over the past few months, most recently at the Forest at Duke in Durham.

Project Manager Mary Beth Bell and Nurse-Interviewer Robin Berger attended the Fall 1999 Meeting of the Association of the North Carolina Cancer Registrars (ANCCR) in Raleigh, where they displayed study information and spoke with cancer registrars from across the state during meeting breaks. Dr. Schildkraut was also there to answer questions about the study's goals and objectives.

In February, Mary Beth and Nurse-Interviewer Nancy Fisher attended a "Sweetheart Tea" at Women's Hospital in Greensboro, hosted by the North Carolina Chapter of the National Ovarian Cancer Coalition. The "tea" was held to raise awareness in the Triad area of the resources available to ovarian cancer patients and their families.

We also plan to attend the Spring meeting of ANCCR on April 27, 2000 in Burlington. We hope the cancer registrars will visit our display and pick up a complimentary gift as our thanks for all their efforts on behalf of the North Carolina Ovarian Cancer Study.

NOTE: We would welcome any opportunity to discuss the study with physicians, nurses, or hospitals. Please let us know if you would like us to provide information about the North Carolina Ovarian Cancer Study at upcoming meetings or seminars. ♀

STUDY CONTACT INFORMATION

DUKE COMPREHENSIVE CANCER CENTER

- **Andrew Berchuck, M.D.**
  Professor, Division of Gynecologic Oncology
  (919) 684-3765
  email: berch001@mc.duke.edu

CANCER PREVENTION, DETECTION, AND CONTROL RESEARCH PROGRAM

- **Joellen Schildkraut, Ph.D.**
  Associate Professor
  (919) 681-4761
  email: schil001@mc.duke.edu
- **Mary Beth Bell, MPH**
  Project Manager
  1-888-246-1250
  (919) 681-4554
  email: mary.bell@duke.edu

[redacted]

- **Dale Herman, Director**
  (919) 715-4555
  email: dale.herman@ncmail.net
- **Dianne Vann, Research Associate**
  (919) 715-4560
  email: dianne.vann@ncmail.net

Study Participation—How It Works

- The hospital Cancer Registrar sends monthly information on newly diagnosed ovarian cancer cases to the North Carolina Central Cancer Registry. (If needed, a representative from the Central Cancer Registry can assist with this task).
- The Central Cancer Registry forwards potentially eligible cases to the study project manager for determination of study eligibility.
- A consent form is sent to the attending physician requesting permission to contact their patient.
- When physician consent is received, a letter and brochure describing the study are sent to the patient.
- Shortly thereafter, a nurse-interviewer telephones the patient to discuss the study, determine eligibility, and, if eligible, invite her to participate.
- Hospitals are paid $10 for every eligible case reported to the NC Central Cancer Registry.

September 2000 —Vol. 2, No. 1

North Carolina Ovarian Cancer Study

Rapid-Case Reporting of Primary Peritoneal Carcinoma Begins...

Duke University, as part of the *North Carolina Ovarian Cancer Study*, is now collecting data on women diagnosed with primary peritoneal carcinoma (PPC) in addition to women diagnosed with epithelial ovarian cancer. Primary peritoneal carcinoma is similar to ovarian cancer in embryonic origin of tissues, histology, symptoms, and treatment. In fact, 10% of women originally diagnosed with ovarian cancer are ultimately determined to have primary peritoneal carcinoma. Duke researchers would like to learn more about the similarities and differences between ovarian cancer and primary peritoneal carcinoma especially with respect to risk factors and molecular changes in the DNA of cancerous cells.

Cancer registrars will soon receive a letter requesting that they report primary peritoneal carcinoma cases along with ovarian cancer cases to the North Carolina Central Cancer Registry on a rapid-case ascertainment basis. The continued support of the hospital registrars is greatly appreciated.

PURPOSE OF STUDY:

To identify the environmental, reproductive, and genetic factors that contribute to the development of ovarian cancer.

STUDY PERIOD:

January 1999-2003

PRIMARY PERITONEAL CARCINOMA STATISTICS:

- **Primary peritoneal carcinoma is similar to ovarian cancer in embryonic origin of tissues, histology, symptoms, and treatment.**
- **Ten percent of women originally diagnosed with ovarian cancer are ultimately determined to have primary peritoneal carcinoma.**

P.O.C.A. Begins Second Year!

The Piedmont Ovarian Cancer Association (P.O.C.A.), formerly the North Carolina Chapter of the National Ovarian Cancer Coalition (NOCC-NC), is dedicated to promoting ovarian cancer awareness through education and fundraising. The organization is expanding its media coverage to make women aware of ovarian cancer risk factors, symptoms, possible ways to reduce risk of the disease and sources of other assistance in the community.

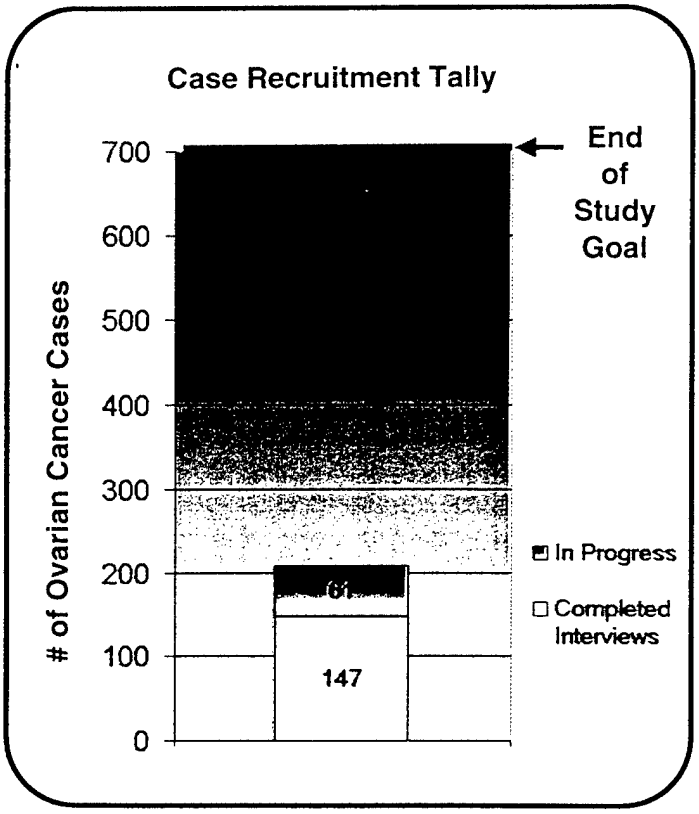
An Awareness Quilt will soon be completed and displayed in area hospitals. The group is also developing educational brochures and audio-visual materials for use at health fairs, physician's offices and women's group gatherings. A financial aid fund (see related article, p. 2, "Run, Run, Run") is also being established to assist ovarian cancer patients and their families with living expenses and the high cost of medical treatment. On September 9, 2000, P.O.C.A. will host the Anne Bagnal Memorial Golf Classic for Ovarian Cancer Awareness in Greensboro, NC.

For more information, contact Kathryn Wilson, Founder/Director, P.O.C.A. Leave a voice mail message at 336-656-0290.

September is National Ovarian Cancer Awareness Month

Also In This Issue...

NCOCS Accrual Report As of August 3, 2000



The response to the *North Carolina Ovarian Cancer Study* among women with ovarian cancer has been tremendous! To date, 90% of the eligible ovarian cancer cases referred to our study have agreed to participate. While the response rate is extremely encouraging and shows how important the study is to women diagnosed with ovarian cancer, we are lagging in our overall goal of completing interviews with 700 ovarian cases over the four-year period from January 1999 through December 2002 (see chart).

Since June 1999, 26 hospitals across our 48-county study region have sent 226 names of eligible women, recently diagnosed with ovarian cancer, to the North Carolina Central Cancer Registry. The Registry in turn forwarded the names to us. If we are to achieve our goal of 700 cases, we will need the continued help of the registrars at these 26 hospitals as well as registrars at other hospitals within the 48-county study region.

Additionally, we plan to complete interviews with 700 women without ovarian cancer over this same four-year period. To date we have identified 208 eligible controls. Their names were obtained through HCFA tapes as well as through a random-digit dialing process.

RUN, RUN, RUN!!!

Women and their families struggling with ovarian cancer often face financial as well as emotional hardships. In her job as Nurse-Interviewer with the *North Carolina Ovarian Cancer Study*, Nancy Fisher has spent a great deal of time talking with these women and has been so moved by the strength and courage they have shown that she wanted to find a way to help. Joining forces with the Piedmont Ovarian Cancer Association (see related article, p.1), Nancy established the P.O.C.A. Hope Fund specifically to assist ovarian cancer patients and their families who are experiencing financial hardships.

Nancy also wanted to find a way to raise money for the Hope Fund. Although not a serious runner, she decided that running a marathon could be a way to raise money for this cause. Hearing that Raleigh was putting together the first Annual Fulcrum Raleigh Marathon on December 3, 2000, she registered, and began training for a 26.2 mile run. Her preparation also includes obtaining sponsorship for her fund from friends, relatives, and others interested in supporting the P.O.C.A. Hope Fund. Her personal goal is to honor these extraordinary women by raising $15,000 to kick off the fund. One hundred percent of the money she raises will be used to assist ovarian cancer patients and their families in North Carolina. This is one of the first ovarian cancer patient assistance funds of its kind in North Carolina.

Nancy is soliciting donations for this worthy cause from both individuals and corporations. If you would like more information about this fundraising effort, please contact Nancy Fisher at 1-888-246-1250, or by e-mail at fishe002@mc.duke.edu. Tax-deductible contributions made **payable to the Piedmont Ovarian Cancer Association** can be sent to:

Nancy Fisher
Box 2949 DUMC
Durham, NC 27710

Active **Consent**

Are We Losing Potential Participants?

Rapid Case Ascertainment

Overall, the rapid-case ascertainment system has been very successful in helping us to identify and recruit women into the *North Carolina Ovarian Cancer Study*. In most hospitals, registrars identify women with ovarian cancer within two months of diagnosis and send their names to the North Carolina Central Cancer Registry, which then forwards the names to the *North Carolina Ovarian Cancer Study* researchers.

Active Consent

The Institutional Review Boards at a handful of hospitals in the 48-county study area have agreed to participate in the study only if patients are enrolled through a process called "active consent." This means that hospital personnel (usually the registrars) must first contact patients, not to obtain their consent to participate in the study, but to determine their willingness to have their names sent to study personnel by the North Carolina Central Cancer Registry. This process is designed to protect patients' privacy.

Challenges of Active Consent

In practice, however, the active consent process has many challenges and places extra burdens on patients and registrars alike. This process also reduces the number of eligible women who participate in the study, partly by requiring an extra step in the enrollment process for patients and partly by requiring extra work on the part of the registrars. In some cases, patients must sign and return a letter to the hospital stating that they are willing to have their name forwarded to the researchers by the North Carolina Central Cancer Registry. In other cases, they are asked to provide consent to hospital personnel over the phone. Registrars are extremely busy people and, understandably, often do not have the time to follow up on unanswered letters or to try to reach patients at various times during the day. As a result, some women who might be eligible for the study are not reached. Furthermore, registrars may not be able to answer all the questions a patient may ask about the study, which may deter prospective participants. Without strict protocols in place requiring physician consent prior to contacting patients, it is also possible that women might inadvertently be contacted about the study prior to learning about their cancer diagnosis from their physician.

Solutions to Challenges

As researchers, we have developed procedures to avoid these potential problems. We have designed standardized protocols that ensure that all prospective participants are treated in the same manner from the start to the completion of the study. We follow up on unanswered letters and call patients at various times of the day, evening, and weekend so that all potentially eligible women have the opportunity to participate in the study. This is important because we want our study results to reflect the experiences of all women with epithelial ovarian cancer. To help women decide whether or not to enroll in the study, our nurses are trained to answer questions about the study. We are careful to send invitation letters to potential participants only after assessing basic eligibility requirements (e.g. age, county of residence) and receiving permission from the patients' doctors.

Women enrolled in the *North Carolina Ovarian Cancer Study* have been eager to participate to help find the causes of ovarian cancer. It is only through a well-designed study which includes all eligible participants that we can identify risk factors for this deadly disease and determine how best to prevent future cases.

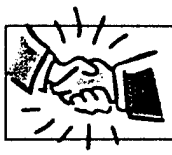
Visit One of the Following Websites to Learn More About Ovarian Cancer During September, Ovarian Cancer Awareness Month:

Gynecological Cancer Foundation
www.wcn.org/gcf

National Ovarian Cancer Coalition
www.ovarian.org

Women's Cancer Network
www.wcn.org

OncoLink: Ovarian Cancer
www.oncolink.upenn.edu



A Letter of Thanks

Study researchers at Duke University Medical Center's Cancer Prevention, Detection, and Control Research Program are very grateful for the efforts of cancer registrars across the 48-county region who are participating in rapid-case reporting of primary epithelial ovarian cancer cases. Your help in providing this information in a timely fashion to the Central Cancer Registry has been essential in allowing us to identify and interview women who have been recently diagnosed with this life-threatening disease. Reaching these women as soon as possible after diagnosis is of utmost importance to the study, and we thank you for going the extra mile to help us in our efforts.

Study Participation- How It Works

- The hospital Cancer Registrar sends monthly information on newly diagnosed ovarian cancer cases to the North Carolina Central Cancer Registry. (If needed, a representative from the Central Cancer Registry can assist with this task).
- The Central Cancer Registry forwards potentially eligible cases to the study project manager for determination of study eligibility.
- A consent form is sent to the attending physician requesting permission to contact their patient.
- When physician consent is received, a letter and brochure describing the study are sent to the patient.
- Shortly thereafter, a nurse-interviewer telephones the patient to discuss the study, determine eligibility, and, if eligible, invite her to participate.
- Hospitals are paid $10 for every eligible case reported to the NC Central Cancer Registry.

STUDY CONTACT INFORMATION

DUKE COMPREHENSIVE CANCER CENTER

- **Andrew Berchuck, M.D.**
  Professor, Division of Gynecologic Oncology
  (919) 684-3765
  email: berch001@mc.duke.edu

CANCER PREVENTION, DETECTION, AND CONTROL RESEARCH PROGRAM

- **Joellen Schildkraut, Ph.D.**
  Associate Professor
  (919) 681-4761
  email: schil001@mc.duke.edu
- **Mary Beth Bell, MPH**
  Project Manager
  1-888-246-1250
  (919) 681-4554
  email: mary.bell@duke.edu

[redacted]

- **Dale Herman, Director**
  (919) 715-4555
  email: dale.herman@ncmail.net
- **Dianne Vann, Research Associate**
  (919) 715-4560
  email: dianne.vann@ncmail.net

CORRECTION

In our last newsletter, we omitted Wilson Memorial Hospital from the list of participating hospitals. We apologize for this omission and thank Wilson Memorial Hospital IRB staff and cancer registrar for their participation.

Biographical Sketches

Provide the following information for the key personnel listed on page 1 of the Detailed Cost Estimate form for the initial budget period.

NAME	POSITION TITLE
Jeffrey R. Marks, Ph.D.	Associate Professor

EDUCATION/TRAINING (Begin with baccalaureate or other initial professional education, such as nursing, and include post-doctoral training.)

INSTITUTION AND LOCATION	DEGREE (IF APPLICABLE)	YEAR(S)	FIELD OF STUDY
University of Chicago	B.A.	1973-77	Biology
University of California, San Diego	Ph.D.	1979-85	Biology
Princeton University	Post-Doc	1985-88	

RESEARCH AND PROFESSIONAL EXPERIENCE: Concluding with present position, list, in chronological order, previous employment, experience, and honors. Include present membership on any Federal Government public advisory committee. List, in chronological order, the titles, all authors, and complete references to all publications during the past 3 years and to representative earlier publications pertinent to this application. If the list of publications in the last 3 years exceeds two pages, select the most pertinent publications. PAGE LIMITATIONS APPLY. DO NOT EXCEED THREE PAGES FOR THE ENTIRE BIOGRAPHICAL SKETCH PER INVESTIGATOR.

Fellowships:

1979	National Institute of Health, Pre-Doctoral Fellowship
1985	Anna Fuller Fund Post-Doctoral Fellowship
1986	American Cancer Society, Post-Doctoral Fellowship

Job History:

1988-94	Assistant Research Professor, Duke University, Surgery Dep't
1994-1998	Associate Research Professor, Duke University, Surgery Dep't
1998	Associate Professor, Duke University, Surgery Dep't
1999	Director, Breast Cancer Research Program, Duke Comp. Cancer Center

Relevant Qualifications for Directing a Virtual Center of Research Excellence in Breast Cancer

I have been an active cancer biology scientist since 1985 and I have been working on the molecular biology of breast cancer since 1988. I have worked very closely with clinicians, epidemiologists, statisticians, behavioralists, and informatics experts in developing my own research and in creating breast cancer programs at Duke. I was co-director of the Duke Breast Cancer SPORE and took over full direction of this effort in June of 1999. I recently completed a full-scale competetive renewal of this program which includes diverse components of translational science, all dedicated to breast cancer. My work with clinicians has given me a broad understanding and appreciation of the many issues of prevention, diagnosis, and treatment of the disease. I recently competed successfully for an Early Detection Research Grant to discover novel markers for the early detection of breast cancer. In

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